REMARKS

Claims 5-11 and 14-16 are pending in the present application.

Applicants wish to thank Examiner Tran for the helpful and courteous discussion with their undersigned Representative on July 27, 2004. During this discussion, several arguments were discussed to overcome the rejections over the art of record. The content of this discussion is reflected by the amendments and remarks set forth herein.

The rejections of (a) Claims 5-10 and 15 under 35 U.S.C. §103(a) over Gram et al in view of Pecht et al and the Examiner's interpretation of the specification at page 3, lines 19-22, and (b) Claims 11-12 and 16 under 35 U.S.C. §103(a) over Gram et al in view of Pecht et al and the Examiner's interpretation of the specification at page 3, lines 19-22, and Barbas et al, are traversed.

The present invention provides a method for *in vitro* detection of a gene encoding a drug-targeted protein, comprising

linking an antigenic substance to a drug via a chemical cross-linker to form a probe, wherein the drug is non-protein and *per se* exhibits no antigenicity and wherein the antigenic substance is serum albumin or fluorescein isothiocyanate and wherein the chemical cross-linker is selected from the group consisting of glutaraldehyde, hexamethylene diisocyanate, hexamethylene diisothiocyanate, N,N'-poly(methylene)bis(iodoacetamide), N,N'-ethylenebis(maleimide), ethylene glycol bis(succinimidyl) succinate, sulfosuccinimidyl-4-(p-maleimidophenyl) buryrate, and bisdiazobenzidine;

screening for the gene encoding a protein targeted by said drug, wherein said protein is expressed from a cDNA expression library containing genes of an organism to which the

drug is to be administered, by using an antigen-antibody reaction between the antigenic substance of the probe and a labeled antibody specific for the antigenic substance; and

determining the gene sequence of the protein expressed from the cDNA expression library within the probe-bound is contained in a phage vector (see Claim 5).

Gram et al disclose a method for *in vitro* detection of monoclonal antibodies from a combinatorial library that bind to a progesterone-bovine serine albumin conjugate. However, Applicants submit that this disclosure cannot affect the patentability of the claimed invention.

First, Applicants note that the present invention is fundamentally different from the disclosure of Gram et al. Although the Examiner cites this reference for disclosing a method for *in vitro* detection of a gene encoding a drug-targeted protein, Applicants disagree. Applicants note that at no point do Gram et al disclose or suggest that their progesterone-bovine serum albumin conjugate is used to detect genes of the target protein in a living body. The methods of Gram et al are limited to phage display methods. Pecht et al is cited for showing cross-linkers for bifunctional reporters; however, the bifunctional reporters disclosed by Pecht et al are for immunoprecipitation methods. As is widely appreciated, phage display and immunoprecipitation are completely distinct methods, which operate in virtually opposite manners (*i.e.*, one requires intact cell membranes, while the other requires lysed cells in order to operate). Accordingly, in view of the significant divergence in the techniques of Gram et al and Pecht et al, there would be no motivation to combine the disclosures of these references; much less any expectation that the bifunctional reporters disclosed by Pecht et al may be used with the substances disclosed by Gram et al (*i.e.*, progesterone and bovine serum albumin).

Moreover, as conceded by the Examiner, Gram et al is silent with respect to the specific cross-linking agents in previously Claim 5 from which the remaining claims depend. Where Gram et al is cited for disclosing a probe for phage-display containing progesterone

(*i.e.*, "drug") cross-linked to BSA, Pecht et al and the disclosure in the present specification at page 3, lines 19-22 are cited to show that the claimed cross-linkers (*e.g.*, glutaraldehyde) are commonly used to cross-link "drugs" to BSA. Barbas et al is cited as disclosing the use of nitrocellulose filters with isopropyl-b-D-thiogalactopyranoside to capture a phage from plated phage culture. However, even if the skilled artisan were to combine the disclosures of the Gram et al, Pecht et al, the Examiner's interpretation of the specification at page 3, lines 19-22, and Barbas et al the combined disclosures still fail to compensate for the basic deficiency in the disclosure of Gram et al (see above).

MPEP §2142 states: "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation... to modify the reference... Second, there must be a reasonable expectation of success. Finally, the prior art reference... must teach or suggest all the claim limitations." Based on the foregoing, it is clear that in view of the combined teachings of Gram et al, Pecht et al, the Examiner's interpretation of the specification at page 3, lines 19-22, and Barbas et al, in any combination, these references would fail to disclose or suggest each limitation in the claim and that the inventive method may be used to ascertain the genes of the target protein in a living body.

Accordingly, Applicants request withdrawal of this ground of rejection.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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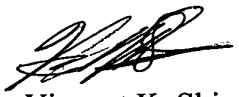

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